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FOUND IN TRANSLATION

# Surmounting structural barriers to tackle endemic infectious diseases

Felix Calderón<sup>1</sup>, Alan H. Fairlamb<sup>2</sup>, Mike Strange<sup>1,4</sup>, Pauline Williams<sup>1,4</sup>, and Carl F. Nathan<sup>3</sup>

**A unique experiment in bringing academic and industrial scientists together to tackle endemic infectious diseases has proved a success. The Tres Cantos Open Lab Foundation, guided and advised by independent experts, funds extended stays of academics at the campus of a pharmaceutical company, where they access the firm's resources in partnership with company scientists. Progress in tackling tuberculosis, protozoal infections, and enteric bacterial diseases has sustained the decade-long evolution of the model, whose distinctive features complement other public-private partnerships with similar goals.**

Malaria, tuberculosis, Chagas disease, leishmaniasis, and enteric bacterial infections disproportionately affect low- and middle-income countries. The substantial global burden of these diseases demands increased drug development. However, difficulties faced by academic innovators in gaining access to industry-grade expertise and resources in drug discovery are key structural barriers to progress (Davis et al., 2021). The conventional form of interaction was inefficient: scientists might report their discoveries to their institutional technology transfer offices, and drug developers might license the discoveries. Thereafter, there would be little communication or mutual education between the academics and industry scientists. The past decade has seen different organizational experiments to increase the efficiency of such interactions focused on diseases whose burdens fall most heavily on low- and middle-income countries. Examples include the Medicines for Malaria Venture, Drugs for Neglected Diseases Initiative, and the Drug Accelerators for tuberculosis and malaria, established by the Bill and Melinda Gates Foundation, which link members of academic and industrial sectors in virtual networks for structured collaboration.

Here we describe a complementary approach to overcoming structural barriers to drug development for endemic infectious diseases—the Open Lab innovation model. The Open Lab supports collaborative residencies for academics within a pharmaceutical company. Established in 2010 by GlaxoSmithKline (GSK), the Open Lab model has proven its utility and durability over the last decade (GlaxoSmithKline, 2010). A companion article in *Nature Reviews Drug Discovery* describes the Open Lab's scientific accomplishments (Calderón et al., 2021). Here we describe the Open Lab's approach and the organizational structure that sustains it.

The Open Lab is an experimental collaborative initiative centered at GSK's Tres Cantos R&D Campus in Spain, offering researchers in endemic infectious diseases access to GSK's core capabilities and expertise in drug discovery (Tres Cantos Open Lab Foundation, 2019b). Unlike the Drug Accelerators, where membership is by invitation, anyone can apply to the Open Lab. In contrast to the Medicines for Malaria Venture, Drugs for Neglected Diseases Initiative, and the Drug Accelerators, the Open Lab involves extended, person-to-person engagement between academics and industry

scientists colocated in the same laboratory at a pharmaceutical company campus. The academic team retains ownership of the project, and any intellectual property arising from the Open Lab projects must be shared in a “knowledge pool” with publication of key data supporting drug discovery.

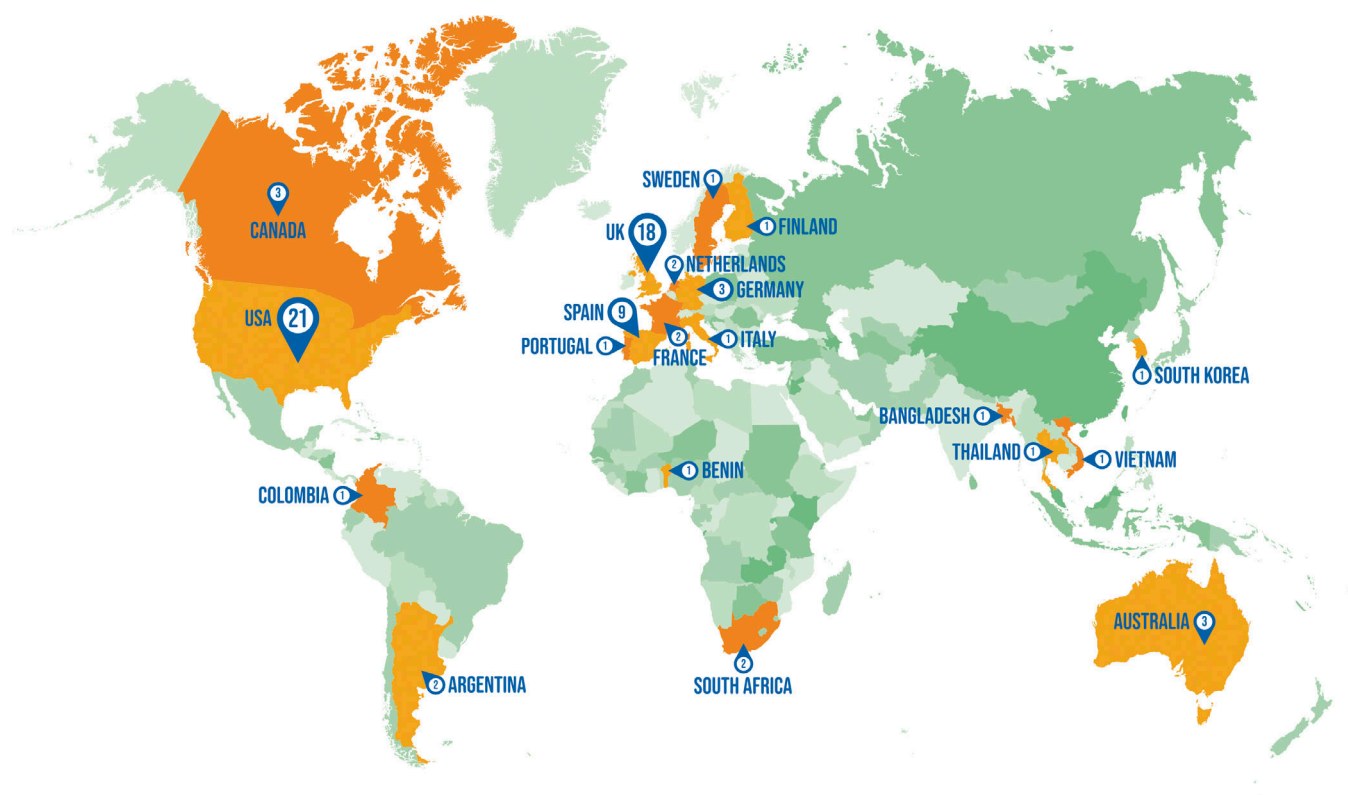
Projects are selected for the Open Lab by the Tres Cantos Open Lab Foundation (TCOLF), a charity established in the UK and governed by an independent board of directors. TCOLF provides funding to cover salaries, accommodation, travel expenses, and relocation services for academics whose projects are selected. GSK provides administrators, scientists, and technical staff who engage with the project teams, along with covering in-kind research costs for laboratory space, equipment, materials, and support services.

An independent scientific board of infectious disease experts reviews Open Lab applications (Tres Cantos Open Lab Foundation, 2019a). Projects are evaluated with respect to the following four parameters: (1) high quality innovation—the application must be scientifically thorough and rigorous, show clear objectives, and introduce new ideas, methods, or hypotheses; (2) feasibility—there must be a clear plan for

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Distribution of institutions that have participated in the Open Lab model.

progression at the Open Lab; (3) significance—there must be a reasonable prospect for a positive impact on the global health pipeline; and (4) alignment with the Open Lab concept and policies—the proposal needs to explain how the project will benefit from on-site collaboration with an industry-based team, and the applicant's institution must accept Open Lab policies regarding intellectual property and publication.

The Open Lab aims to bridge the translational gap between fundamental scientific exploration and the discovery of new medicines, spanning the so-called “valley of death” where 90% of promising ideas for clinical intervention are lost (Barohn et al., 2019; Seyhan, 2019; Truebel and Thurston, 2020). As the relationship between fundamental and applied research has matured, the nature of accepted proposals has evolved. At first, the selected projects focused on discovering early drug candidates. Later, priorities broadened to include methods for shortening treatments, tools for supporting disease eradication, novel drug combinations, disruptive target-based programs, validation of new phenotypes, and the development of more physiologically relevant disease models.

Before projects reach the Open Lab, GSK scientists offer a period of less formal collaboration to allow for the exchange of ideas and guide the design of more competitive proposals. Informally termed “pre-Open Lab,” this can include experimental work, proof-of-concept studies, or simulations. This period is critical not just to generate data, but to define clear objectives and engender alignment for collaborative success. Cross-disciplinary teamwork and the desire to solve real-world problems that impact patients are the most important factors in ensuring progress.

Most Open Lab fellows are postdoctoral scientists from academia. Although the Open Lab is not designed as a training program, the experience advances investigators' scientific education, provides visibility of opportunities available in both industry and academia, and fosters a new generation of global health scientists with wide-ranging knowledge of their field and an awareness of the capabilities of industry to deliver new medicines.

Key to the Open Lab approach is the alignment of its activities to best serve the community. This is encompassed within three main areas. (1) Intellectual property.

All Open Lab projects follow the principles of World Intellectual Property Organization (WIPO) Re:Search, a public-private partnership administered by WIPO in collaboration with BIO Ventures for Global Health (<https://www.wipo.int/research/en/>).

WIPO Re:Search allows organizations to share their intellectual property, expertise, facilities, and know-how royalty-free with qualified researchers worldwide working on new solutions for neglected tropical diseases, malaria, and tuberculosis. (2) Collaborator colocation. The usual model of industry-academia collaborations is based on combining the technical expertise of each partner and sharing information in meetings and in written form. In contrast, the Open Lab allows colocation of researchers from each organization in the same laboratory in Tres Cantos. This catalyzes the exchange of ideas and information, enhancing the thriving scientific community in Tres Cantos by bringing diversity of thought and culture and enriching the collaborative experience. Informal exchange of ideas on a day-to-day basis allows any issues to be addressed promptly. Although communications within a particular project are extensive, conversations among investigators from

different institutions have been more cautious, perhaps reflecting an academic culture of prepublication competition. Because expanding cross-project interactions is likely to be fruitful, the Open Lab is striving to create a sheltered environment for the safe intermingling of different project groups. (3) Financial independence. The TCOLF board of directors independently decides where and when to invest. GSK has provided financial support to TCOLF—a total of £15 million in three tranches (2010, 2012, and 2018). Applications are straightforward, comprising responses to 11 questions. With three TCOLF Board meetings a year, applications receive feedback and a decision within 4 mo. These provisions ensure that investigators are not burdened with excessive administrative requirements and that there is flexibility within the system to make rapid decisions on funding so that projects are not delayed.

The orientation of the Open Lab toward providing the best possible experience for investigators has driven high demand, with more than 85 projects approved and implemented since 2011, coming from 75 different institutions in 20 countries. Over 100 academic scientists have progressed their projects, benefiting from access to GSK's screening platforms, medicinal chemistry, ADMET tests (absorption, distribution, metabolism, excretion, and toxicology), animal models, assay development expertise, and target validation platforms. In particular, the Open Lab offers investigators opportunities

not available at many academic institutions, such as biosecurity level 3 in vitro and in vivo laboratories and an insectary. These efforts have resulted in the publication of hundreds of validated hits, the characterization of structure–function relationships for more than 20 novel chemical scaffolds, including a novel clinical candidate, as well as the evaluation of drug-repurposing opportunities. Moreover, the innovative nature of the projects has required the development of novel screening assays, discovery platforms, and in vitro and in vivo models.

This year marks 10 yr since the first Open Lab project started. It has been a decade of transformation in global health. We now have clear mandates that define the scientific agenda across neglected infectious diseases. Accomplishing this agenda requires us to depart from conventional models of drug and vaccine development and continually reevaluate our policies, processes, and approach to risk. It is uncommon for any industry initiative to last for 10 yr, even more so if it involves collaboration. For example, within the TB Drug Accelerator, which is likewise celebrating its 10th anniversary, there have been changes in the list of participants from the pharmaceutical sector along the years (Aldridge et al., 2021). Moreover, even with the rapidly evolving nature of the industry with periodic review of priorities—and GSK is no exception—the Open Lab has persisted and thrived.

The Open Lab continues to surprise and deliver as a rapid testbed for new ideas and as a unique experiment in effective cross-disciplinary collaboration. Ongoing challenges include the adaptation of the model to accommodate projects aligned with needs in the field and to increase the geographical diversity of applications. Looking ahead to the next 10 yr, we envisage the prophylactic and therapeutic pipeline for endemic infectious diseases continuing to increase in scope and quality and to deliver new tools and approaches that improve human health around the globe.

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